Claims 60-77, presented hereby in place of claims 38-59, are pending.

Claims 60-63 contain subject matter of claims 38-40 and 56, respectively, claims 64 and 65 contain the subject matter of claim 57, and claims 66 and 67 contain the subject matter of claims 58 and 59, respectively, amended to more clearly define the invention.

More specifically, claim 38 is amended as claim 60 to include the sequence identifier "SEQ ID NO: 1." The subject matter of claims 57-59 is rewritten, hereby, in method of use format, as claims 64-67, with the language "pharmaceutical containing a composition according to claim 38" recited in claim 57 changed to "pharmaceutical composition containing a compound according to claim 60" in present claim 64, and with the subject matter appearing in parenthesis in claim 57 being made the subject matter of new claim 65, which is dependent on claim 64.

Claims 69-73, added hereby, are composition claims, supported by the original claims and, also, e.g., in the specification paragraph bridging pages 12 and 13.

The objection to the specification and claims because of the missing sequence identifier is overcome by the instant amendment.

An objection in the Office Action maintains that the amino acid sequence appearing in the specification and claims must be replaced using a 3-letter code for each amino acid, instead of the single-letter code used. The objection is mistaken; in accordance with MPEP 2429 (*emphasis added)*:

> **Helpful Hints for Compliance** . . .
> - *Single letter* amino acid abbreviations are not acceptable within the Sequence Listing but *may appear elsewhere in the application.*

Claims 41-55 were rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite, and under 35 U.S.C. §102(b) as allegedly being anticipated by WO 91/11457 (Buckley). The rejections against claims 41-55 are rendered moot by cancellation of the claims, hereby.

Claims 57-59 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Reconsideration is requested.

According to the statement of rejection, claim 57 is indefinite for reciting the "composition of claim 38," when claim 38 defines a "compound." The rejection against claim 57 is overcome by the instant amendment, in that none of the present claims refer to a parent "compound" claim as a *composition*.

Claim 57 is, further, allegedly indefinite for containing subject matter appearing in parentheses. The instant amendment overcomes this reason for the rejection of claim 57, in that none of the present claims contain subject matter appearing in parentheses. Subject matter that appear in parentheses in claim 57 is, by the instant amendment, made the subject matter a separate, dependent claim (claim 70).

Claims 57-59 were rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Reconsideration is requested in view of the replacement claims submitted, hereby, in conjunction with the following remarks.

According to the statement of rejection, enablement is lacking allegedly because "undue experimentation would be required to characterize the involvement of the claimed GLP-1 proteins in each specific disease and determine what form of administration and what dosage would be

effective to treat each specific disease." (Office Action, page 8). The allegation of "undue experimentation" is mistaken.

First of all, the "pharmaceutical composition" recited in the present claims, i.e., method-of-use claims 69-71 is limited to the peptide having sequence GLP-1(7-34), i.e., the compound of present claim 60. Thus, the enablement requirement of §112, paragraph 1, is satisfied as long as "any person skilled in the art" is enabled by the present specification "to make and use" the peptide GLP-1 (7-34) in the treatment of the pathological conditions recited in these claims (claims 69-72).

As acknowledged in the statement of rejection (Office Action, page 6), the present specification is "enabling for a pharmaceutical containing a compound according to claim 38 for the therapy of insulin-independent diabetes mellitus." Accordingly, the only issue raised in the rejection under §112, paragraph 1, as applied against the present claims at issue (claims 64-68) is whether the present specification

> reasonably provide(s) enablement for pharmaceuticals containing the compound [GLP-1 (7-34)] . . . . for the therapy of insulin-dependent diabetes mellitus, MODY (maturity-onset diabetes in young people), secondary hyperglycaemias in connection with pancreatic diseases (chronic pancreatitis, pancreatectomy, or haemochromatosis), endocrine diseases (acromegaly, Cushing's syndrome, phaeochromocytoma, or hyperthyerosis[), hyperglycaemias induced by drugs (benzathiadiazine salidiuretics, diazoxide, or a glucocorticoids), pathologic glucose tolerance, hyperglycaemias, dyslipoproteinaemias, obesity, hyperlipoproteinaemias, and/or hypotonias.

(Office Action, page 6.) In the present case enablement is shown because screening a protein, i.e., the compound GLP-1 (7-34), for biological activity is routine, not undue, experimentation. *Ex parte Mark*, 12 USPQ2d 1904 (BPA&I 1989).

Reconsideration is requested with respect to the rejection of claims 38-40 and 56-59 under 35 USC 102(b) based on Danley and the rejection of claims 30 and 56-59 based on Habener.

Danley (EP 0 619 322) also discloses GLP-1 peptides such as 7-37, 7-36, 7-35, as well as 7-34 (page 2, line 4). Sequence no. 5 shows an amino acid sequence similar to the peptide presently claimed, but without the amide modification at the C-terminus. The reference points out that modifications at the C-terminus were disclosed in the prior art (see page 2, line 33 and 54). There is pointed out that derivatives of polypeptides include polypeptides having inconsequential amino acid substitutions, or additional amino acids to enhance coupling to carrier protein or to enhance the insulinotropic effect thereof. Further derivatives of insulinotropin disclosed in such reference include certain C-terminal salts, esters and amides where the salts and esters are defined as OM where M is a pharmaceutically acceptable cation or a lower branched or unbranched alkyl group and the amides are defined as -NR2R3 where R2 and R3 are the same or different and are selected from the group consisting of hydrogen and a lower branched or unbranched alkyl group.

For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp.* To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis*

added). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

Danley does not specifically describe the GLP-1 (7-34) amide presently claimed, nor does it teach or suggest that the GLP-1 (7-34) amide is the preferable peptide modification for gaining more insulinotropic effect. Thus, Danley does not anticipate the subject matter of the claims.

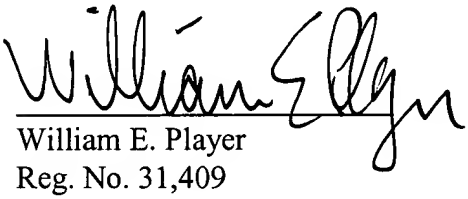
Basically the same applies to the reference Habener (US5,118,666). Also Habener is silent with respect to the specific GLP-1 [7-34 amide].

Attached hereto are graphically represented data, which show how various GLP-1 derivatives, i.e., specifically, GLP-1 [7-34 amide], GLP-1 [7-37], and GLP-1 [7-37 amide], differ with respect to cAMP binding. The graph clearly shows that the compound presently claimed, i.e., GLP-1 [7-34 amide], exhibits a very steep increase in cAMP binding between 10^{-9}-10^{-8} M or, in other words, very high potency. The comparative data show that the GLP-1 (7-34) amide possesses unexpected potency with respect to the other peptides tested. Therefore, the GLP-1 (7-34) amide is novel over the other peptides tested.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: 
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APPENDIX

Marked-up Version of Amendment

IN THE SPECIFICATION:

Rewrite the paragraph bridging pages 6 and 7 as:

In particular, those derivatives derived from GLP-1-(7-34)COOH and the corresponding acid amide are employed which have the following general formula:

R-NH-HAEGTFTSDVSSYLEGQAAKEFIAWLVK-$CONH_2$ (SEQ ID NO:1),

wherein R = H or an organic compound having from 1 to 10 carbon atoms. Preferably, R is the residue of a carboxylic acid. Particularly preferred are the following carboxylic acid residues: formyl, acetyl, propionyl, isopropionyl, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl.